201-15019

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Michael Leavitt, Administrator
U.S. Environmental Protection Agency
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Washington, DC 20460

PETA
PEOPLE FOR THE ETHICAL TREATMENT OF ANIMALS

HEADQUARTERS
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Re: Comments on the API's Test Plan for the Grease Thickeners Category

Dear Administrator Leavitt:

The following comments on the API's High Production Volume test plan for grease thickeners are submitted on behalf of the Physicians Committee for Responsible Medicine, People for the Ethical Treatment of Animals, the Humane Society of the United States, the Doris Day Animal League, and Earth Island Institute. These health, animal protection, and environmental organizations have a combined membership of more than ten million Americans.

The grease thickeners test plan presents a review of the chemistry and toxicity of these non-toxic, non-bioavailable compounds. Several of the compounds in this category are either GRAS compounds (calcium stearate) or very closely related to GRAS compounds. Any new proposed testing should be evaluated in the light of these facts and other data. The EPA has recommended the following with regard to GRAS substances specifically:

> *"In analyzing the adequacy of screening data for chemicals that are substances Generally Recognized as Safe (GRAS) for a particular use by the Food and Drug Administration (FDA), participants should consider all relevant and available information supporting the FDA's conclusions. Participants reviewing the adequacy of existing data for these chemicals should specifically consider whether the information available makes it unnecessary to proceed with further testing involving animals...."* (*Federal Register* Vol. 65, No. 248, December 28, 2000.)

In general, the grease thickeners are organic acid salts of fatty acids. As such, catabolism of fatty acids is a well documented metabolic process (Champe & Harvey, 1994) in animals and humans. Research has established that mammals have enzyme systems capable of metabolizing short, medium, long, and branch chain fatty acids. The metabolic pathway is the same for all chain lengths and does not distinguish between saturated and unsaturated fatty acids. The metabolic product for even numbered fatty acids is acetyl-CoA (or acetate). These compounds fall within the molecular range of fatty acids normally metabolized by animals and humans, and have no structural characteristics that would indicate that they require toxicity testing.

Despite this very low documented toxicity, the API is proposing to conduct a combined reproductive/developmental test (OECD 421) on a single substance (lithium hydroxystearate in a grease matrix) which will result in the deaths of at least 675 animals.

The low toxicity of the compounds in this group is clear. Many of these compounds are edible, and no effects were observed at very high doses in the repeat dose and acute toxicity studies. At issue, however, is the concern that women being treated with lithium carbonate for manic depression during early pregnancy may have slightly higher risk of having infants with certain congenital defects (Cohen et al 1994, Jacobsen et al 1992, Jacobsen et al 1993) and a higher risk of premature births (Troyer et al 1993), and that exposure to lithium in grease thickeners could result in similar effects. The human lithium studies indicate that, when patients are ingesting sufficient lithium to produce palliative effects for manic-depression, a slight increase in the risk of developmental toxicity is observed. Estimates of the increase in risk of developmental effects are thought to be from a range of 2 to 4% to a range of 4 to 12 % (Cohen et al 1994).

However, the amount of lithium that could be ingested or absorbed from any exposure to these compounds is extremely limited. For example, the lithium content of CAS# 4485-12-5, lithium stearate, is only 1% in the pure substance based on its stoichiometery ($LiC_{35}H_{12}O_2$). As stated in the test plan, this compound or similar compounds make up less from 1-14% of the grease. Since therapeutic doses of lithium to treat manic depression are 1-2 grams of lithium per day, a pregnant woman would have to ingest somewhere between 714 grams to 20,000 grams (1.5 to 44 pounds) of lubricating grease per day in order to ingest the equivalent lithium dose of the therapeutic treatments which have been thoroughly studied for their developmental effects in humans. Furthermore, the bioavailability and solubility of the lithium in these compounds is very low, so that the doses required to absorb a similar amount of lithium compared to therapeutic doses would be much higher. And since ingestion is not the primary pathway for human exposure, the proposed study is for a dermal reproductive/developmental test using a grease with lithium fatty acid salt as a thickener. This route of exposure would even further decrease the likelihood that absorbed doses of lithium would ever approach the high doses required to adversely affect reproductive parameters in humans. This study will therefore not result in any useful information.

In fact, with the existing database on human effects at high levels of lithium, it is inconceivable that further reproductive/developmental tests of non-toxic substances with low levels of lithium in them would provide any useful information regarding the reproductive and developmental effects of these compounds. Again, as stated in the December 2000 *Federal Register* notice on this program, *"In analyzing the adequacy of existing data, participants shall conduct a thoughtful, qualitative analysis rather than use a rote checklist approach. Participants may conclude that there is sufficient data, given the totality of what is known about a chemical, including human experience, that certain endpoints need not be tested."*

Like so many previous API test plans, this one is characterized by a lack of thoughtful toxicology. We are requesting that the API reexamine this proposal and apply thoughtful toxicology rather than condemn yet another 675 animals to suffering and death in this testing plan.

We would appreciate receiving a direct response from the API to our concerns. I can be reached at 757-622-7382, ext. 8001, or via e-mail at JessicaS@peta.org.

Sincerely,

Jessica Sandler
Federal Agency Liaison

References

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